REMARKS

As a preliminary matter, Applicants' undersigned representative thanks the Examiner for indicating that claim 33 is allowed (see, page 1 of the Final Rejection).

I. The Claimed Invention is Novel

Claims 19, 20, 24-29 and 32 are rejected under 35 U.S.C. §102(e) as allegedly being anticipated by U.S. Patent No. 6,713,059 (hereinafter the "Kende reference"). In particular, the Office alleges that Kende discloses: (1) monoclonal antibodies to N-butanoyl-L-homoserine lactone; (2) methods of treating or preventing an infectious disease comprising administering the antibody to a subject; and (3) single chain antibodies. Applicants respectfully disagree.

The Kende reference fails to anticipate claims 19, 20, and 24-29, and 32 because the Kende reference fails to disclose a monoclonal antibody that "specifically binds to the free soluble form of the [antigen] in the presence of conjugated derivatives thereof," as recited in the claims. It is has been submitted previously that the antibodies of the Kende reference. are generated in animals following multiple immunizations with an immunogenic conjugate of a lactone signaling molecule. This approach relies upon generation of antibodies *in vivo* by the immune system of the animal, and is the basis of vaccine development. However, the present application teaches how to generate human antibodies that are specific for the free form (i.e. soluble, non-conjugated form) of a signaling molecule.

The antibodies of the Kende reference are raised against antigens conjugated to a carrier molecule, for example, BSA. By way of background, antibodies are significantly larger than homoserine lactone molecules and because of this size disparity the antibodies will often completely envelop the antigen. Antibodies that bind to the antigen when conjugated to a carrier molecule (such as the type disclosed in the Kende reference.) will ***not*** always and necessarily recognize the soluble free form of the antigen. Since the soluble free form of the antigen is what is found *in vivo,* it is desired to test the ability of any antibodies selected to recognize and bind the soluble free form of the antigen. The Kende reference. fails to show that the antibodies generated bind to the free soluble form of the antigen in contrast to the present claims.

The ability of the antibodies of the current invention to bind the soluble free form of the antigen is demonstrated in the Description. In Example 1 (see page 30, lines 16 to 26 and the results in table 2 on figure sheet 4/12 in particular) a competitive inhibition ELISA assay was used to determine the sensitivity of the antibodies for the soluble free form of the antigen. Please find enclosed a schematic diagram (Exhibit 1) which explains the methodology of this assay.

First, an ELISA plate is coated with antigen conjugated to a carrier molecule (for example, BSA). Second, antibodies of the invention may be added to the agar plate which binds to the antigen-carrier molecule conjugate. Free soluble antigen is then added, and the concentration of soluble antigen required to reduce the binding of the antibody to the conjugate by half (i.e. the IC_{50}) can be determined.

Table 2 in the present application shows that a concentration as low as 11 μM dDHL-COOH was sufficient to reduce the binding of the G3H2 antibody to the conjugate by half. This clearly demonstrates the ability of the antibodies of the invention to bind to the soluble free form of the antigen since the free form of the antigen is able to successfully compete with the conjugate for binding to the antibody. This feature is present in the claims since independent claims 1, 11, 17, 19 and 32 all recite that the antibody is able to "specifically bind to the free soluble form of the [antigen] in the presence of conjugated derivatives thereof."

In contrast, the Kende reference reports antibodies that bind to the conjugated antigen. It does not explicitly disclose antibodies with the ability to bind the free form of the antigen. Therefore, the Kende reference fails to teach each and every element of the claim.

Accordingly, Applicants respectfully assert that the claimed invention is novel and request that this rejection under 35 U.S.C. § 102 be withdrawn.

II. The Claimed Invention is Not Obvious

Claims 1, 2, 6-12, 17-20, 24-29, 32, and 33 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over the Kende reference in view of McCafferty *et al.* (Nature, Vol. 348, No. 6301, pp. 552-554 (1990), hereinafter the "McCafferty reference"). Applicants respectfully disagree.

The claims are not obvious in view of the Kende and McCafferty references because the combination of references fails to yield the present invention. As discussed above, the Kende reference fails to teach a monoclonal antibody that "specifically binds to the free soluble form of the homoserine lactone or a C_1-C_{10} saturated or unsaturated carboxylic acid derivative thereof in the presence of conjugated derivatives thereof," as recited in the present claims. The McCafferty reference fails to cure this deficiency. The McCafferty reference reports phage antibodies but does not disclose or suggest an antibody that can bind to the free soluble form of a homoserine molecule but not to the carrier to which the same molecule can be conjugated.

In addition, when combining the teachings of the Kende reference with the McCafferty reference, the skilled person is not led to reproduce the invention, that is the production of antibodies that can bind to the soluble free form of the antigen in the presence of conjugated derivatives thereof, as recited by independent claims 1, 11, 17, 19 and 32. In the McCafferty reference, whilst describing the principle of using naive human phage display libraries to generate antibodies, the McCafferty reference does ***not*** provide a person of skill in the art with the necessary teaching to generate antibodies to the free soluble form of an antigen when considered with the teaching of the Kende reference.

As the Office notes, a rigid application of the Court of Appeals for the Federal Circuit's TSM test was rejected by the Supreme Court, but the Supreme Court did state that to support an obviousness finding there must be an articulated reason. As the M.P.E.P. states, "[the key to supporting any rejection under 35 U.S.C. 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious." (M.P.E.P. § 2141). "[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *Id.* The Office has failed to put forward a sufficient articulated reason as to why claims the claims are obvious in view of the prior art. Even if combined, the Kende reference and the McCafferty reference fail to disclose the subject matter recited in the pending claims. The Office has failed to point to any reason as to why the references would be modified to produced the claimed invention as recited in the claims. Therefore, because the Kende and McCafferty references fail to teach an antibody that specifically binds to the free soluble form of the homoserine lactone or

a C_1-C_{10} saturated or unsaturated carboxylic acid derivative thereof in the presence of conjugated derivatives thereof the rejected claims are not obvious.

In view of the foregoing, Applicants respectfully request that the rejection of claims under 35 U.S.C. §103(a) be withdrawn.

III. Conclusion

Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited. The Examiner is invited to contact Applicants' undersigned representative at (610) 640-7820 to resolve any remaining issues.

The Commissioner is hereby authorized to debit any underpayment of fee due or credit any overpayment to Deposit Account No. 50-0436.

Respectfully submitted,

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